PEC UPDATE

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ISSUE HIGHLIGHTS

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Merry Christmas and Happy Holidays from the PEC!

IV Dilantin® Discontinuation

Starting January 1, 1997, Parke-Davis will no longer distribute the intravenous (IV) formulation of phenytoin sodium (Dilantin®). Instead, Parke-Davis will be marketing fosphenytoin injection (Cerebyx®). Fosphenytoin was developed to improve the safety and tolerability issues associated with parenteral phenytoin sodium.[1,2]

Like IV phenytoin sodium, fosphenytoin is indicated for acute treatment and control of generalized status epilepticus, and for treatment and prophylaxis of seizures occurring during neurosurgery. Additionally, IV or intramuscular (IM) fosphenytoin can be used as a short-term substitute for oral phenytoin when oral administration is not feasible.[3] IM administration of phenytoin sodium is not recommended since it results in poor bioavailability, inflammation, hemorrhage, necrosis, and thrombosis at the injection site.[4]

Fosphenytoin is a highly water-soluble, phosphate ester prodrug that is rapidly converted to phenytoin after IV administration. It has a pH of 8.6 to 9.0 compared with a pH of 12.0 for phenytoin sodium. These properties confer less pain and irritation at the infusion site, allow a faster infusion rate, and provide more reliable absorption after IM administration.[2,5]

Fosphenytoin is dosed as phenytoin sodium equivalents (PE) so that conventional dosing guidelines for phenytoin can be directly applied to fosphenytoin.[1,5] A 75 mg dose of fosphenytoin is equivalent to 50 mg of phenytoin sodium.[1,4] Fosphenytoin can be diluted in 5% dextrose or normal saline and administered at a rate up to 150 mg PE/minute.[1,2,4] The goals of therapy for fosphenytoin with regard to therapeutic drug monitoring are the same as those for phenytoin sodium—total phenytoin levels range from 10-20 μg/mL and unbound phenytoin levels range from 1.0-2.0 μg/mL.[5]

Fosphenytoin caused less injection site irritation (9%) and fewer infusion interruptions (21%) compared to phenytoin sodium (90% and 67%, respectively).[1,3] Transient paresthesia (4.4%) and pruritus (48.9%) were more common with IV fosphenytoin. Both of these adverse effects have a frequency of less than 4% with IM administration of fosphenytoin.[2,4] These sensations typically occur over the face and in the groin and are dose and rate related. They do not appear to be allergic reactions and

alone do not warrant discontinuation of therapy.[5] Other adverse effects of fosphenytoin are similar to those of phenytoin sodium. As with phenytoin sodium, cardiac monitoring is recommended during administration of IV loading doses of fosphenytoin.[1,3,4] Additionally, the phosphate load provided by fosphenytoin (0.0037 mmol phosphate/mg PE) should be considered when treating patients requiring phosphate restriction.[4]

Table—Drug Acquisition Price Comparisons

NDC	*Drug*	*Manufacturer*	*DAPA Price**
00071-4007-05	Fosphenytoin 150 mg/2 mL (100 mg PE), 25s	Parke-Davis	$279.30
00071-4008-10	Fosphenytoin 750 mg/10 mL (500 mg PE), 10s	Parke-Davis	$335.16
00071-4488-45	Phenytoin sodium 100 mg/2 mL, 25s	Parke-Davis	$3.45†
39769-0034-02	Phenytoin sodium 100 mg/2 mL, 25s	Solopak	$5.24
00641-0493-25	Phenytoin sodium 100 mg/2 mL, 25s	ESI-Lederle	$7.94
00071-4475-45	Phenytoin sodium 250 mg/5 mL, 25s	Parke-Davis	$4.00†
00641-2555-45	Phenytoin sodium 250 mg/5 mL, 25s	ESI-Lederle	$8.85

*Distribution and Pricing Agreement (DAPA) prices may vary by region.
†to be discontinued as of 1/1/97

Fosphenytoin must be stored under refrigeration at 2°C to 8°C (36°F to 46°F), and should not be stored at room temperature for more than 48 hours.[4] Health care professionals should be aware of these storage requirements since fosphenytoin may not be available in automated dispensing machines, code boxes, crash carts, etc., when an acute need for the drug arises.

Fosphenytoin is more expensive than phenytoin sodium (Table). Although Dilantin® brand IV phenytoin will no longer be available, it is available generically. The generic injectable products listed in the Table are considered to be therapeutically equivalent to other pharmaceutically equivalent products, and there are no known or suspected bioequivalence problems ("AP" rated).[6] No pharmacoeconomic analyses have been conducted to date comparing fosphenytoin to injectable phenytoin sodium.

References:

1. Warner-Lambert *Cerebyx* (fosphenytoin) will be available in September; IV *Dilantin* to be discontinued at year-end: Cerebyx priced at premium to Dilantin. *F-D-C Reports* 1996;58(33):10-1.
2. Fierro LS, Savulich DH, Benezra DA. Safety of fosphenytoin sodium. *Am J Health-Syst Pharm* 1996;53:2707-12.
3. Hydantoins monograph. In: Olin BR, editor. Facts and Comparisons. St. Louis: Facts and Comparisons, Inc., 1996:282d-283b.
4. Fosphenytoin, Pharmacy and Therapeutics Review, 1996 Updated Evaluation. In: Cada D, Selevan J, editors. The Formulary. St. Louis: Facts and Comparisons, Inc., 1996: 365-72.
5. Boucher BA. Fosphenytoin: a novel phenytoin prodrug. *Pharmacotherapy* 1996;16:777-91.
6. United States Pharmacopeial Convention. Approved drug products and legal requirements. USP-DI Vol. III. 16th ed. Rockville, MD: United States Pharmacopeial Convention, Inc., 1996.

Sole Source Selections on the TSF

The PEC has assumed the policy function of designating sole source items for use at military treatment facilities (MTFs). Previously, this function was handled by the Defense Medical Standardization Board (DMSB). The PEC designates the following medications as sole source items on the Tri-Service Formulary (TSF):

- digoxin tablets (Lanoxin®) - Glaxo Wellcome
- carbamazepine tablets (Tegretol®) - Ciba-Geigy
- phenytoin tablets & capsules (Dilantin®) - Parke-Davis

Currently, levothyroxine (Synthroid®) by Boots Pharmaceuticals is a sole source medication. However, the PEC is re-evaluating this sole source selection and will notify MTFs if this selection should change. The Defense Personnel Support Center (DPSC) will only issue DAPA prices for these sole source items.

The TSF sole source items are identified in the updated TSF Quick Reference Guide on page 4 of this PEC Update.

PEC Moving to New Offices

The PEC has outgrown its current office space. We will be moving to a new location on Fort Sam Houston to better accommodate the staff. Although the exact timing of the move is not known as we go to press, we will do our best to keep you, our valued customers, informed of what is happening. At this time, we do not anticipate any changes in telephone numbers. We will notify you of our change of address and any other changes through future PEC Updates, the PEC Home Page on the World Wide Web, and the PEC bulletin board service, as the information becomes available.

PEC Bulletin Board Telephone Numbers

Prefix: COM (210) 221- DSN 471-

Line 1 . . . . . -3371	Line 3 . . . . . -3373
Line 2 . . . . . -3372	Line 4 . . . . . -3374

PEC Home Page Address
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1997 PEC Ambulatory Care Pharmacist Conference

The 1997 Ambulatory Care Pharmacist (ACP) Conference is just around the corner! The conference will be held at the Hilton Palacio del Rio on the Riverwalk in San Antonio, Texas, on January 26-29, 1997. The program is being coordinated through The University of Texas at Austin, College of Pharmacy.

This year's program will focus on assessing and applying therapeutic data to develop disease management programs. Conference attendees also will hear "success stories" from other conference participants. A poster session has been planned to give participants the opportunity to highlight activities at their facilities. An opening reception is planned for the evening of Sunday, January 26, 1997, and a dinner program is planned for the evening of January 28, 1997. Tentative program topics and speakers are listed below.

Attendance at this program is mandated for all ACPs hired to support the PEC initiatives. The PEC will send individual fund-cites to those facilities who have an ACP. Additionally, chiefs of pharmacy, Deputy Commanders for Clinical Services at facilities, P & T Committee chairpersons, lead agents for DOD regions, and pharmacy benefit managers and contractors working with DOD are invited to attend the conference. Pharmacist continuing education credit will be offered. In addition, continuing medical education credit (CME) is being sought for physicians attending the conference. Don't miss this great opportunity to network with other ambulatory care pharmacists and health care providers.

Pharmacists, physicians, and other health care providers interested in attending the conference should contact Eugene Moore, Pharm.D. at the PEC (210-221-5694) or Jill Williams at The University of Texas, College of Pharmacy (512-471-6213, fax 512-471-8783) for additional information.

Tentative Program Topics and Speakers

- Role of the pharmacist in management of diabetics—compliance, monitoring, drug use - Betsy A. Carlisle, Pharm.D.
- Critical review of a civilian based diabetes clinic - Marvin D. Shepherd, Ph.D.
- Current pharmacy profile of the DOD diabetic patient population - James Wilson, Ph.D.
- Workshop on building a disease management program - Marvin D. Shepherd, Ph.D., James Wilson, Ph.D.
- Credentialing process for pharmacists - Edward Jai, Pharm.D.
- Persuasive skills for communicating to other health care practitioners - John Daly, Ph.D.
- Utilization of CHCS databases - Maj. William Hasewinkle
- Implementation of guidelines and therapeutic protocols - Scott Weingarten, M.D., M.P.H.
- Formulary decision making and DOD PEC models and operation - Melvin Miller, R.Ph.
- CliniTrend™ software demonstration - Jillmarie Yanchick, Pharm.D.

Tri-Service Formulary Quick Reference Guide

Antimicrobials / Antifungals
*amoxicillin oral suspension and caps
*Bactrim™/Septra® susp and tabs
*dicloxacillin oral
*doxycycline 100 mg caps
*erythromycin oral suspension and tabs or caps
*erythromycin/sulfisoxazole susp
*griseofulvin 125 mg tabs
*isoniazid 300 mg tabs
*metronidazole 250 mg tabs
*nystatin oral suspension
*penicillin VK susp and 250 mg tabs
*rifampin 300 mg caps
*tetracycline 250 mg caps

Antibiotics-EENT
*Cortisporin® Otic Suspension
*gentamicin ophth. soln. 0.3%
*Neosporin® Ophth. Solution
*sulfacetamide ophth. oint. 10%

Antivirals
acyclovir 200 mg caps

Anthelmintics
mebendazole 100 mg chew tabs

Antiulcer Drugs
*amoxicillin oral
*bismuth subsalicylate 262 mg tabs
*metronidazole 250 mg tabs
*tetracycline 250 mg caps

GERD Agents
cisapride 20 mg tabs
omeprazole 20 mg caps

Other GI Agents
*dicyclomine tabs or caps
*Donnatal® tabs
*sulfasalazine 500 mg tabs

Anti-diarrheals
*loperamide 2 mg tabs or caps

Genitourinary Agents
*oxybutynin 5 mg tabs
*phenazopyridine 100 mg tabs

Gout Agents
*allopurinol tabs
*probenecid 500 mg tabs

Muscle Relaxants
*diazepam 5 mg tabs
*methocarbamol 500 mg tabs

Oral Corticosteroids
*prednisone 5 & 20 mg tabs
prednisone oral soln 5 mg/5 mL
prednisolone oral soln 15 mg/5 mL

Nasal Corticosteroids
*beclomethasone nasal inhaler

Asthma Agents
*albuterol oral inhaler
flunisolide oral inhaler
triamcinolone oral inhaler
*theophylline liquid 80 mg/15 mL
SloBid™ Gyrocaps 50, 200, 300 mg

Antihistamines / Decongestants
*Actifed® tabs
*chlorpheniramine 4 mg tabs
*chlorpheniramine syrup
*Dimetapp® Elixir
*Dimetapp® Extentabs
*diphenhydramine caps
*diphenhydramine syrup
*hydroxyzine syrup
*hydroxyzine tabs
*oxymetazoline nasal spray
*pseudoephedrine 30 mg tabs

Anticonvulsants
†Dilantin® Infatabs 50 mg
†Dilantin® Kapseals 100 mg
*phenobarbital elixir 20 mg/5 mL
*phenobarbital 30 mg tabs
*primidone 250 mg tabs
†Tegretol® 200 mg tabs

Anticoagulants
warfarin 5 mg tabs

Diuretics
*furosemide 40 mg tabs
*hydrochlorothiazide tabs
*Maxzide® tabs
*spironolactone 25 mg tabs

Vasodilators
*isosorbide dinitrate 10 mg tabs
nitroglycerin sublingual tabs

Lipid Lowering Agents
colestipol powder
*niacin tabs
pravastatin 10 mg, 20 mg, 40 mg tabs

Hypotensive / Cardiac Drugs
*atenolol tabs
*clonidine tabs
†Lanoxin® 0.25 mg tabs
lisinopril tabs
*propranolol 10 & 40 mg tabs
*quinidine gluconate 324 mg tabs
*quinidine sulfate tabs
terazosin tabs
*verapamil long-acting tabs

Electrolyte Replacement
*potassium chloride slow release tabs or caps

Diabetic Agents
*human insulin, regular & NPH

NSAIDS / Analgesics
*acetaminophen drops, elixir, and 325 mg tabs
*aspirin, enteric-coated 325 mg tabs
*ibuprofen susp and 400 mg tabs
*indomethacin 25 mg caps
*Tylenol #3® tabs

Migraine Agents
*Cafergot® tabs
*Fiorinal® tabs
*Midrin® caps

Attention Deficit / Narcolepsy Agents
*methylphenidate 10 mg tabs
*methylphenidate sustained release 20 mg tabs

Contraceptives
LoOvral®
*Norinyl 1+50®, Ortho-Novum 1/50®
*Ortho-Novum 1/35®, Norinyl 1+35®
Ortho-Novum 7/7/7®
Ovral®
Triphasil®/Tri-Levlen®

Estrogens / Progestins
conjugated estrogens 0.625 mg tabs
conjugated estrogen vaginal cream
*medroxyprogesterone 10 mg tabs

Thyroid / Antithyroid Agents
*propylthiouracil 50 mg tabs
†Synthroid® 100 mcg (0.1 mg) tabs

Topical Agents
*bacitracin ointment
*hydrocortisone 1% cream
*miconazole 2% topical cream
Sebutone® shampoo
*Selsun® shampoo

Vaginal Antifungal Agents
clotrimazole 500 mg vaginal tab

Vitamins & Minerals
*ferrous sulfate concentrated soln. 125 mg/mL
*ferrous sulfate 325 mg tabs
*pyridoxine 50 mg tabs

Miotics
*pilocarpine ophth. solution

Miscellaneous
insect sting kit
InspirEase® spacer

**** generic products are available***
† sole source item

Brand names are included for example only and are not meant to imply the recommendation of a specific product except for those products designated as sole source items by the Pharmacoeconomic Center

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